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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/541,195	06/30/2005	Patricia Salvati	373987-004US (396982)	7746

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EXAMINER	
JAVANMARD, SAHAR	

ART UNIT	PAPER NUMBER
1617	

MAIL DATE	DELIVERY MODE
09/18/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/541,195	SALVATI ET AL.	
	Examiner	Art Unit	
	SAHAR JAVANMARD	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 May 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5,9,10,12-14 and 16-23* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5,9,10,12-14 and 16-23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *5/21/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of the Application

This Office Action is in response to applicant's arguments filed on 05/21/2008. Claim(s) 1-5, 9-10, 12-14 and 16-23 are pending. Claim(s) 6-8 have been cancelled. Claim(s) 16-23 have been added. Claim(s) 1-5, 9-10, 12-14 and 16-23 are examined herein.

Response to Arguments

Amendments to the claims and specification are hereby acknowledged.

In view of Applicant's amendments of claims 1-10 and 12-14 with respect to the 112 1st rejection, the rejection is hereby withdrawn.

Applicant's amendments of claims 1-4, 6-10, 12 and 13 with respect to the 102(b) rejection as being anticipated by Pevarello (WO 99/35125) have been fully considered but are not persuasive. Examiner maintains that pain is pain, no matter the mechanism by which it occurs. Thus treating head pain conditions involving "a cerebral vasodilation mechanism, wherein the head pain conditions are both primary and secondary" is not of patentable weight. Thus the 102(b) rejection is maintained for claims 1-4, 9-10, 12 and 13 for reasons of record, but is modified as necessitated by Applicant's amendments. Claims 6-8 were cancelled.

Applicant's arguments with respect to the 103(a) rejection of claims 5 as being obvious over Pevarello (WO 99/35125) have been fully considered but are not

persuasive. Similar to the 102(b) rejection above, Examiner maintains that pain is pain, no matter the mechanism by which it occurs. Thus the 103(a) rejection is maintained for reasons of record but is modified as necessitated by Applicant's amendments.

Applicant's arguments with respect to the 103(a) rejection of claim 14 as being obvious over Pevarello (WO 99/35125) in view of Lan (WO 99/26614) have been fully considered and upon further consideration the following new non-final 103(a) rejection of claim 14 is now made.

Claim Rejections - 35 USC § 102

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-4, 9-10, 12, 13 and 19-22 are rejected under 35 U.S.C. 102(b) as being anticipated by Pevarello et al. (WO 99/35125).

Examiner respectfully notes that treating head pain conditions involving "a cerebral vasodilation mechanism, wherein the head pain conditions are both primary and secondary" is not of patentable weight. Pain is pain, no matter the mechanism by which it occurs,

Pevarello teaches compounds of formula I and pharmaceutically acceptable salt thereof (page 2, line 2- page 5, line 26) as therapeutic agents used for treating pain associated with damage or permanent alteration of the peripheral or central nervous systems such as peripheral neuropathies e.g. trigeminal and post-therapeutic

neuralgia, diabetic neuropathy, glossopharyngeal neuralgia, radiculopathy, neuropathy secondary to metastatic infiltration, adiposis dolorosa and burn pain and central pain conditions such as those following stroke, thalamic lesions and multiple sclerosis (page 6, lines 13-22). Thus the limitations of claims 1-4, 9-10 and 20 are met.

Pevarello further discloses a dosing regimen where the compounds of interest, specifically (S)-2-[4-(3-fluorobenzyloxy)benzylamino]-propanamide, were administered in doses of 7.5, 15.0, 30.0 and 60.0 mg/kg (page 12, lines 20-26), meeting the limitations of claims 12 and 13.

Pavarello teaches that said compounds are useful in mammals, including humans, as analgesic agents (page 15, lines 5-6), meeting the limitations of claim 19.

The compounds can be administered in a variety of dosage forms including orally, rectally and parenterally (page 16, lines 5-9), meeting the limitations of claims 21 and 22

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein

were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claim 5 and 16-18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Pevarello et al. as applied to claims 1-4, 9-10, 12, 13 and 19-22 above.

Pevarello is discussed above.

Pevarello teaches (S)-2-[4-(3-fluorobenzyloxy)benzylamino]-propanamide however does not specifically teach the (+) optical isomer as recited in claim 5.

As per claims 17 and 18, 2-[4-(2-fluorobenzyloxy)benzylamino]-propanamide and 2-[4-(3-chlorobenzyloxy)benzylamino]-propanamide are taught, respectively, however Pevarello does not specifically teach the S-(+) optical isomer.

It would have been prima facie obvious to one of ordinary skill in the art at the time of the invention to have known that the (S) racemate of 2-[4-(3-fluorobenzyloxy)benzylamino]-propanamide as taught by Pevarello is a mixture of (+) and (-) isomers. Furthermore, one of ordinary skill in the art would also have known that 2-[4-(2-fluorobenzyloxy)benzylamino]-propanamide and 2-[4-(3-chlorobenzyloxy)benzylamino]-propanamide are a mixture of enantiomers in which each enantiomer further comprises of two optical isomers.

The fundamentals of optical activity and stereoisomerism are well known to persons having ordinary skill in the art. A person having ordinary skill in the art would have known how to resolve the racemic mixture and would have been motivated to do so with the reasonable expectation of achieving enantiomers having substantially different pharmacological activity. It appears as though applicant has determined experimentally what a person of ordinary skill in the art would have expected, namely, that the racemic mixture of the prior art may be separate (+) and (-) enantiomers possessing substantial different pharmacological activity. This is an expected result. It is well established that expected beneficial results are evidence of obviousness of a claimed invention just as unexpected beneficial results are evidence of unobviousness. *In re Skoll*, 523 F. 2d 1392, 187 U.S.P.Q. 481 (C.C.P.A. 1975); *In re Skoner*, 517 F. 2d 947, 186 U.S.P.Q. 80 (C.C.P.A. 1975); *In re Gershon*, 372 F. 2d 535, 152 U.S.P.Q. 602 (C.C.P.A. 1967);

Claim 14 is rejected under 35 U.S.C. 103(a) as being unpatentable over Pevarello et al. as applied to claims 1-4, 9-10, 12, 13 and 19-22 above.

Pevarello is discussed above.

Pevarello does not teach a dose range from 0.5-5 mg/kg.

It would have been obvious to one of ordinary skill in the art at the time of the invention to have administered the drugs taught by Pevarello in the dose range of 0.5-5 mg/kg. The dosage regimen of the compounds of interest is deemed to be a

manipulatable parameter practiced by a person skilled in the art to obtain the best possible range depending the on the route of administration and the weight of the subject.

Claim 23 is rejected under 35 U.S.C. 103(a) as being unpatentable over Pevarello et al. as applied to claims 1-4, 9-10, 12, 13 and 19-22 above.

Pevarello is discussed above.

Pevarello does not teach specifically teach a head pain condition wherein the condition is migraine.

It would have been obvious to one of ordinary skill in the art at the time of the invention to have also administered the compounds employed by Pevarello to have also treated migraine as the disorder. Pevarello teaches treating trigeminal and post-therapeutic neuralgia which are both head pain disorders, therefore one would also be motivated to treat migraines as it is also a head pain disorder.

Conclusion

Claims 1-5, 9-10, 12-14 and 16-23 are not allowed.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only.

For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SAHAR JAVANMARD whose telephone number is (571) 270-3280. The examiner can normally be reached on 8 AM-5 PM MON-FRI (EST).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on (571) 272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

/S. J./

Examiner, Art Unit 1617

/SREENI PADMANABHAN/

Supervisory Patent Examiner, Art Unit 1617